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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,322	10/18/2007	David R. Milich	643802000203	3500

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,322	MILICH ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *170-172,176-178,188-193 and 195-197* is/are pending in the application.

4a) Of the above claim(s) *176-178,189,191,193,195 and 197* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *170-172,188,190,192 and 196* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 170-172, 176-178, 188-193, and 195-197 are pending in the application.

2. In the prior action, mailed on February 26, 2009, claims 170-172, 174-178, and 188-197 were pending in the application; with claims 175-178, 189, 191, 193-195, and 197 withdrawn from consideration; and claims 170-172, 174, 188, 190, 192, and 196 under consideration and rejected.

3. In the Response of August 26, 2009, the Applicant amended claims 170, 176, and 190; and cancelled claims 174, 175, and 194.

4. Claims 170-172, 188, 190, 192, and 196 are under consideration.

5. The action is made Non-Final in view of the new grounds of rejection.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. **(New Rejection)** Claims 170-172, 188, 190, 192, and 196 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods wherein the core particles is one of the core particles identified as being capable of assembly in Table 15 of the application, does not reasonably provide enablement for the claimed methods of use for any rodent hepadnaviral core protein particle as claimed for the production of an immune response against any antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to perform the invention

commensurate in scope with these claims. In particular, the claims are rejected for lacking adequate support to enable the production of hybrid particles required to perform the full scope as permitted by the present claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

These claims are drawn to methods for producing an immune response comprising the administration to an animal (esp. a human having pre-existing anti-HBV antibodies) of a composition comprising a hybrid particle comprising a fusion protein of a rodent (esp. ground squirrel) hepadnavirus core protein and a heterologous antigen, and an expression vector encoding the fusion protein. Claims 171 and 172 specify the immune responses to be induced, and claim 196 specifies that the C-terminal sequence of the core protein is replaced by 1-100 amino acids that is not a single cysteine or wild-type C-terminal sequence of a hepadnaviral core antigen.

It is noted that, in response to the prior art rejections of the prior action, the Applicant has presented arguments and evidence that the prior art was not enabling for the production of fusion

proteins such as those claimed wherein any hepadnaviral core protein was fused with any antigen. It is further noted that the arguments of the Applicant indicate that it was shown that the present application has shown that fusions which failed in the prior art were made to work when one of a select group of provided C-terminal sequences was used to replace the wild-type core protein C-terminal sequence. See e.g., Peterson declaration (section 4.), and specification, pages 114-116. However, it is noted that, even using these disclosed C-terminal sequences, failures where seen. Specification, page 118 (Table 11). Moreover, while the application lists the insertion sites, antigens, and C-terminal sequences used, it is noted that the application does not indicate that any of such antigens may be inserted into any position of any hepadnaviral core protein comprising any of the C-terminal sequences with an expectation that an immunogenic hepadnaviral core particle may be produced.

It is noted that there is no requirement in the present claims that the antigen be inserted at one of the insertion sites identified as effective, no limitation on the antigens that may be inserted, and no requirement for the use of the specific C-terminal sequences actually used in the examples of the specification. As the application indicates at least that the C-terminal sequences coupled with the indicated insertion sites are required, the present claims are therefore rejected as exceeding the scope for which an enabling disclosure has been provided.

It is additionally noted that on pages 114-115, the specification indicates that there are actually at least three variables that must be matched in order to produce an immunogenic core particle: the antigen, the position of insertion, and the C-terminal sequence. As indicated by the teachings of Table 11, certain combinations of these elements, such as the combination of a different antigen with a previously successful insertion site and C-terminal sequence, results in

the inability to produce an immunogenic particle. Thus, the teachings of the present application indicate that outside of the specific examples provided, there is uncertainty as to which antigenic sequences may be inserted into a core protein comprising any particular of the indicted C-terminal sequence, and as to where in such proteins the antigenic sequence may be inserted, so as to result in a particle to be used in the presently claimed methods.

Moreover, the teachings of the application also indicate that there is a further variable adding further unpredictability to the claimed method. Table 15 of pages 122 and 123 indicate that even the hepadnaviral core protein used may affect the ability to make an operable particle. This table demonstrates that the same epitope may be inserted in the same corresponding position of different hepadnaviral core antigens with the same C-terminal sequences with differing results. I.e., the insertion of the epitope into one such core protein may result in the production of a hybrid particle, whereas insertion into a different core protein may fail to do so. Moreover, contrary to the Applicant's assertions on page 10 of the response, the teachings of Table 15 fail to indicate that insertions into a woodchuck core antigen would be any more or less predictive of results of insertions into a ground squirrel core antigen that would insertions of the antigen into a human core antigen. See esp. combinations 8 and 12 of Table 15 (showing that one particle position/antigen/ C-terminal combination successful in a woodchuck core antigen was not successful in a human or ground squirrel core antigen; and that another such combination was successful in human and ground squirrel core antigens, but not in a woodchuck core antigen). Thus, the teachings in the application demonstrate several points on uncertainty even with respect to the use of the antigens, insertion positions, and C-terminal sequences disclosed in the present application. Even with respect to those specifically disclosed combinations shown to

work in one core protein, there is unpredictability as to whether they would result in useful particles when used to attempt to make a similar particle based on a different hepadnaviral core protein.

In view of the Applicant's arguments regarding the lack of enablement for the making of the hybrid particles required to perform the claimed methods, the lack of any limitation in the present claims to limit the particles to be used to those shown to work in the present application, and the unpredictability even with respect to the use of any particular antigen/insertion position/C-terminal sequence combinations (not to mention as to the core particle itself), the claims are rejected as lacking adequate enabling support for the full scope of the claimed methods.

Claim Rejections - 35 USC § 102

8. **(Prior Rejection- Withdrawn)** Claims 170-172 were rejected under 35 U.S.C. 102(b) as being anticipated by Paoletti et al. (Vaccine 20:370-76). In view of the amendment of the claims to require the use of a rodent hepadnaviral core antigen, and exclude the use of the duck hepadnaviral core antigen as disclosed by the applied reference, the rejection is withdrawn.

9. **(Prior Rejection- Withdrawn)** Claims 170-172, 174, 190, 192, and 196 were rejected under 35 U.S.C. 102(a) as being anticipated by Birkett et al. (U.S. 2003/0054337). Applicant's arguments are found persuasive in part (see the obviousness rejection below). The anticipation rejection is therefore withdrawn.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. **(Prior Rejection- Withdrawn)** Claim 188 was rejected under 35 U.S.C. 103(a) as being unpatentable over Paoletti et al. (supra). In view of the amendment of the claims to require the use of a rodent hepadnaviral core antigen, and exclude the use of the duck hepadnaviral core antigen as disclosed by the applied reference, the rejection is withdrawn.

12. **(Prior Rejection- Maintained)** Claims 170-172, 174, 188, 190, 192, and 196 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birkett et al. (supra) in view of the teachings of Paoletti et al. (supra) and of Maruyama et al. (Gastroenterol 106:1006-15) and Shödel et al. (Vaccine 11:624-28). Claim 174 has been cancelled from the application. The rejection of this claim is therefore withdrawn.

The Applicant traverses the rejection on the basis that, because of the differences between the human and rodent hepadnaviral core proteins. The argument is not found persuasive. First, it is noted that the teachings of the Birkett reference itself suggests that the rodent viral core proteins may be substituted for the human core proteins. In addition, the teachings of each of Paoletti and of Shödel indicate that the core antigens of other hepadnaviruses would also be immunogenic. Thus, those of ordinary skill in the art would have had a reasonable expectation of

success in the use of such non-human (including the rodent) core particles as means for the induction of immune responses against at least some antigens as suggested by Birkett.

With respect to the arguments presented in traversal of the anticipation rejection over Birkett, it is noted that, while those of ordinary skill in the art may not have had a reasonable expectation of success in the use of ground squirrel hepatitis virus core protein based particles as a mans for the induction of an immune response against any heterologous antigen, the teachings of the reference indicate that the human virus core proteins had been adapted to induce immune responses against at least certain antigens, such as the malaria antigens in the particles described on pages 25-27 of the Birkett reference. In view of the teachings of the Birkett reference, and the suggestion that the antigens could be also inserted into the core proteins of other hepadnaviral core proteins, those of ordinary skill in the art at the time that the application was filed would have had a reasonable expectation in the making of such particles using the ground squirrel hepatitis virus rather than the human hepatitis B virus. The evidence presented by the Applicant fails to demonstration that those of ordinary skill in the art, at the time that the present application was filed, would not have had such an expectation of success. Nor does the evidence presented by the Applicant indicate that the malaria antigens described by Birkett could not have been used in non-human hepadnaviral core proteins as taught by that reference.

For these reasons, and for the reasons of record, the Applicant's arguments are not found persuasive and the rejection is maintained.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. **(Prior Rejections- Withdrawn)** Claims 170-172 and 174 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 14-28 of U.S. Patent No. 7,320,795. Claim 188 was rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 14-28 of U.S.

Patent No. 7,320,795 in view of the teachings of Paoletti et al. (supra) and of Maruyama et al. (Gastroenterol 106:1006-15) and Shödel et al. (Vaccine 11:624-28).

Claims 170-172, 174, 192, and 196 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32, 36-44, 47-64 of copending Application No. 12/008059. Claim 188 was provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32, 36-44, 47-64 of copending Application No. 12/008059, further in view of Paoletti et al. (supra), Maruyama et al. (supra), and Shödel et al. (supra).

In view of the terminal disclaimer of August 26, 2009, each of the above rejections is withdrawn.

16. **(New Rejection)** Claims 170-172, 188, 190, 192, and 196 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 31-44 of copending Application No. 11/635271; claims 31-88 of copending application No. 11/635275; and of claims 32, 36-44, and 47-64 of copending application number 12/008059. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims are drawn to compositions that are used in the presently claimed methods, and wherein the presently claims methods are disclosed in the specification of the copending application. See e.g., pages 93-94 of the copending application.

This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a

method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert B. Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648